



DNA base oxidation: A Car-Parrinello molecular dynamics study of thymine in the gas and aqueous phase

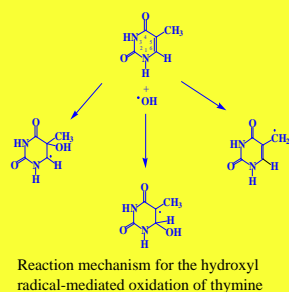
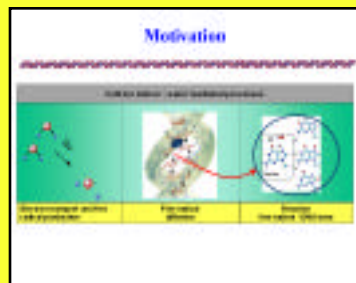
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INTRODUCTION



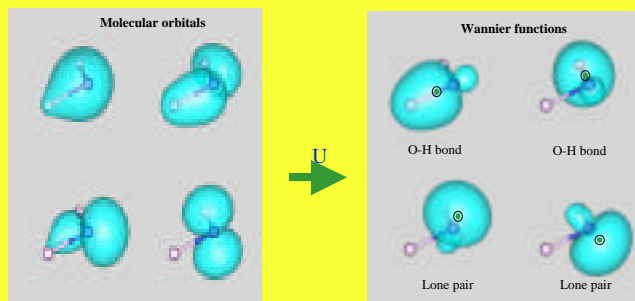
Hydroxyl radicals are likely the main species responsible for oxidative DNA damage in biological systems. The hydroxyl radical-mediated oxidation of bases would be the first step, which is followed by a fast reaction with molecular oxygen and eventually leads to DNA damages, such as mutagenesis.

METHODS

Car-Parrinello Molecular Dynamics is used to explore atomic dynamics. In this approach, the forces on the atoms are derived "on the fly" from the instantaneous ground state of the electrons. The electronic ground state is treated within the framework of density functional theory, using the generalized gradient approximation for exchange and correlation effects. Valence electrons are treated with Vanderbilt ultrasoft pseudopotentials.

Maximally localized Wannier function is calculated along the trajectory to provide the detail of electron movement.

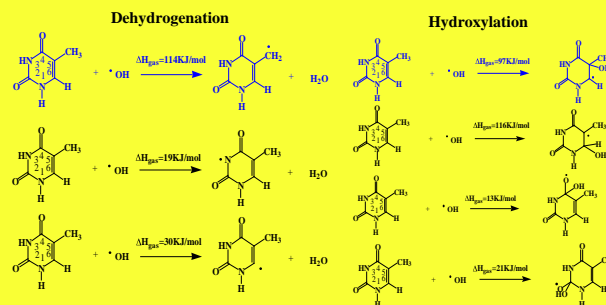
Why Wannier function?



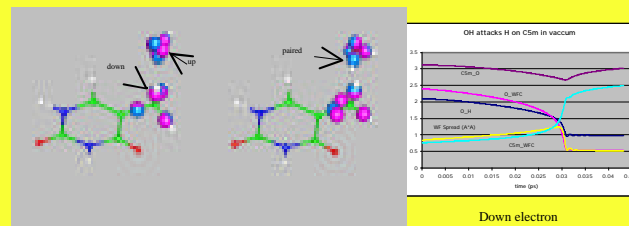
More chemical intuitive and suitable for dynamical study (centroid and spread)

RESULTS

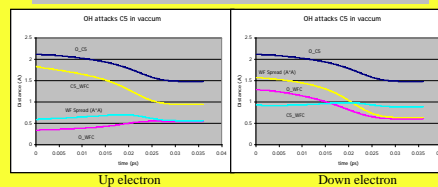
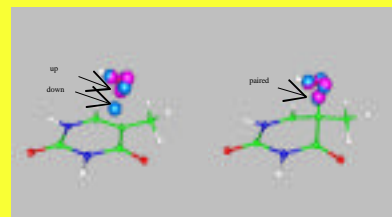
In the gas phase



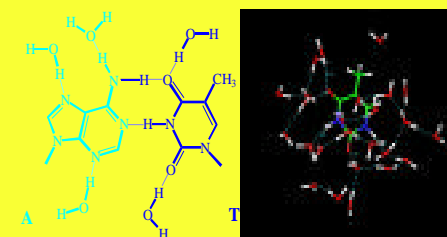
Dehydrogenation in the gas phase



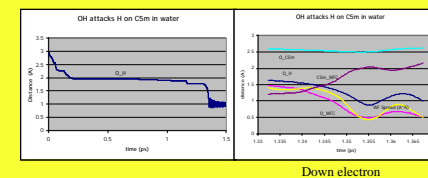
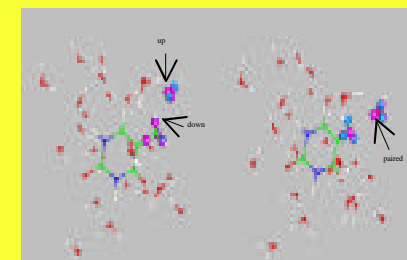
Hydroxylation in the gas phase



In the aqueous phase



Dehydrogenation in the aqueous phase



SUMMARY

- The main reactions of hydroxyl radicals with thymine involve addition to the C₅, C₆ positions and hydrogen abstraction from the C₅ methyl group.
- Both nuclear and electronic motion are dynamically tracked during the chemical reaction. In the dehydrogenation reaction, a electron from the O-H bond pairs with the unpaired electron on OH radical. In the hydroxylation reaction, a electron pairs with the unpaired electron on OH radical.
- The reactions of hydroxyl radical with thymine are diffusion controlled. The reaction mechanism is the same in the gas phase as that in the condensed phase. But the diffusion rate of the hydroxyl radical depends on the environment.